



A DOCPHOENIX

## APPL PARTS

IMIS
Internal Misc. Paper
LET
Misc. Incoming Letter

371P  
PCT Papers in a 371 Application

A...  
Amendment Including Elections

ABST  
Abstract

ADS  
Application Data Sheet

AF/D  
Affidavit or Exhibit Received

APPENDIX  
Appendix

ARTIFACT  
Artifact

BIB  
Bib Data Sheet  
15/03/02 CLM 12  
Claim

COMPUTER  
Computer Program Listing

CRFL  
All CRF Papers for Backfile

DIST  
Terminal Disclaimer Filed

DRW  
Drawings

FOR  
Foreign Reference

FRPR  
Foreign Priority Papers

IDS  
IDS Including 1449

NPL  
Non-Patent Literature

OATH  
Oath or Declaration

PET.  
Petition

RETMAIL  
Mail Returned by USPS

SEQLIST  
Sequence Listing

SPEC  
Specification

SPEC NO  
Specification Not in English

TRNA  
Transmittal New Application

CTNF  
Count Non-Final

CTRS  
Count Restriction

EXIN  
Examiner Interview

M903  
DO/EO Acceptance

M905  
DO/EO Missing Requirement

NFDR  
Formal Drawing Required

NOA  
Notice of Allowance

PETDEC  
Petition Decision

## OUTGOING

CTMS
Misc. Office Action

1449  
Signed 1449

892  
892

ABN  
Abandonment

APDEC  
Board of Appeals Decision

APEA  
Examiner Answer

CTAV  
Count Advisory Action

CTEQ  
Count Ex parte Quayle

CTFR  
Count Final Rejection

## INCOMING

AP.B  
Appeal Brief

C.AD  
Change of Address

N/AP  
Notice of Appeal

PA..  
Change in Power of Attorney

REM  
Applicant Remarks in Amendment

XT/  
Extension of Time filed separate

BACKFILE DOCUMENT INDEX SHEET

### Int rnal

SRNT  
Examiner Search Notes

CLMPTO  
PTO Prepared Complete Claim Set

ECBOX  
Evidence Copy Box Identification

WCLM  
Claim Worksheet

WFEE  
Fee Worksheet

### File Wrapper

FWCLM  
File Wrapper Claim

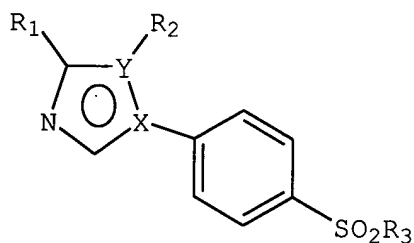
IIFW  
File Wrapper Issue Information

SFRW  
File Wrapper Search Info

6/26/03

Clean Copy of Amended Claims:

1. (Amended) A compound of formula I:



I .

wherein:

one of  $X$  or  $Y$  represents  $N$  and the other represents  $C$ ;

*Al*  
 $R_1$  represents hydrogen, methyl, halogen, cyano, nitro,  $-CHO$ ,  $-COCH_3$  or  $-COOR_4$ ;

$R_2$  represents aryl or heteroaryl unsubstituted or substituted with one or more groups independently selected from halogen,  $C_{1-8}$  alkyl,  $C_{1-8}$  haloalkyl,  $R_4OC_{0-8}$  alkyl,  $R_4SC_{0-8}$  alkyl, cyano, nitro,  $-NR_4R_6$ ,  $-NR_4SO_2R_5$ ,  $-SOR_5$ ,  $-SO_2R_5$ ,  $-SO_2NR_4R_6$ , or  $-CONR_4R_6$ ;

$R_3$  represents  $C_{1-8}$  alkyl,  $C_{1-8}$  haloalkyl or  $-NR_4R_6$ ;

$R_4$  represents hydrogen,  $C_{1-8}$  alkyl, or aryl $C_{0-8}$  alkyl (where the aryl group can be unsubstituted or substituted with one or more groups selected from  $C_{1-8}$  alkyl, halogen,  $C_{1-8}$  haloalkyl, cyano, nitro,  $R_7OC_{0-8}$  alkyl,  $R_7SC_{0-8}$  alkyl,  $-NR_7R_8$ ,  $-NR_7COR_5$ ,  $-COR_7$  or  $-COOR_7$ );

$R_5$  represents  $C_{1-8}$  alkyl or  $C_{1-8}$  haloalkyl;

$R_6$  represents hydrogen,  $C_{1-8}$  alkyl, aryl $C_{1-8}$  alkyl (where the aryl group can be unsubstituted or substituted with one or more groups selected from  $C_{1-8}$  alkyl, halogen,  $C_{1-8}$  haloalkyl, cyano, nitro,

*a1*  
R<sub>7</sub>OC<sub>0-8</sub> alkyl, R<sub>7</sub>SC<sub>0-8</sub> alkyl, -NR<sub>7</sub>R<sub>8</sub>, -NR<sub>7</sub>COR<sub>5</sub>, -COR<sub>7</sub> or -COOR<sub>7</sub>), -COR<sub>8</sub> or -COOR<sub>8</sub>;

R<sub>7</sub> represents hydrogen, C<sub>1-8</sub> alkyl or benzyl;

R<sub>8</sub> represents C<sub>1-8</sub> alkyl or C<sub>1-8</sub> haloalkyl;

aryl in the above definitions represents phenyl or naphthyl; and heteroaryl in the above definitions represents pyridine, pyrazine, pyrimidine or pyridazine, which can be optionally fused to a benzene ring; or a salt, solvate or prodrug thereof.

---

*a2*  
4. (Amended) A compound according to claim 1 wherein R<sub>2</sub> represents phenyl or pyridine unsubstituted or substituted with one or more groups independently selected from halogen, C<sub>1-8</sub> alkyl, C<sub>1-8</sub> haloalkyl, R<sub>4</sub>OC<sub>0-8</sub> alkyl, R<sub>4</sub>SC<sub>0-8</sub> alkyl, cyano, nitro, -NR<sub>4</sub>R<sub>6</sub>, -NR<sub>4</sub>SO<sub>2</sub>R<sub>5</sub>, -SOR<sub>5</sub>, -SO<sub>2</sub>R<sub>5</sub>, -SO<sub>2</sub>NR<sub>4</sub>R<sub>6</sub>, or -CONR<sub>4</sub>R<sub>6</sub>.

---

10. (Amended) A compound according to claim 9 wherein R<sub>2</sub> represents phenyl or pyridine unsubstituted or substituted with one or more groups independently selected from halogen, C<sub>1-8</sub> alkyl, C<sub>1-8</sub> haloalkyl, R<sub>4</sub>OC<sub>0-8</sub> alkyl, R<sub>4</sub>SC<sub>0-8</sub> alkyl, cyano, nitro, -NR<sub>4</sub>R<sub>6</sub>, -NR<sub>4</sub>SO<sub>2</sub>R<sub>5</sub>, -SOR<sub>5</sub>, -SO<sub>2</sub>R<sub>5</sub>, -SO<sub>2</sub>NR<sub>4</sub>R<sub>6</sub>, or -CONR<sub>4</sub>R<sub>6</sub>.

---

*a3*  
11. (Amended) A compound according to claim 1 selected from:

5-(4-fluorophenyl)-1-(4-methylsulfonylphenyl)imidazole;

5-(4-methylphenyl)-1-(4-methylsulfonylphenyl)imidazole;

5-(2,4-difluorophenyl)-1-(4-methylsulfonylphenyl)imidazole;

1-(4-methylsulfonylphenyl)-5-phenylimidazole;

5-(3,4-dichlorophenyl)-1-(4-methylsulfonylphenyl)imidazole;

5-(4-methoxyphenyl)-1-(4-methylsulfonylphenyl)imidazole;

5-(3-fluoro-4-methoxyphenyl)-1-(4-methylsulfonylphenyl)imidazole;

5-(3-fluorophenyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(3-fluoro-4-methylphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(2-fluorophenyl)-1-(4-methylsulfonylphenyl)imidazole;  
1-(4-methylsulfonylphenyl)-5-(4-trifluoromethoxyphenyl)imidazole;  
5-(6-methyl-3-pyridyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(2-fluoro-4-methoxyphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(3-chloro-4-methylphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(3-methoxy-4-methylphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(4-chlorophenyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(6-chloro-3-pyridyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(2,6-dichloro-3-pyridyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(2-chloro-6-methoxy-3-pyridyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(5,6-dichloro-3-pyridyl)-1-(4-methylsulfonylphenyl)imidazole;  
1-(4-methylsulfonylphenyl)-5-(4-propoxyphenyl)imidazole;  
5-(3,5-diethoxyphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(4-ethoxyphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
1-(4-methylsulfonylphenyl)-5-(4-nitrophenyl)imidazole;  
5-(4-methylsulfonylphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(4-ethylsulfonylphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(4-dimethylaminophenyl)-1-(4-methylsulfonylphenyl)imidazole;  
1-(4-fluorophenyl)-5-(4-methylsulfonylphenyl)imidazole;  
5-(4-fluorophenyl)-4-methyl-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(4-fluorophenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(4-methylphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(2,4-difluorophenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-1-(4-methylsulfonylphenyl)-5-phenylimidazole;  
4-chloro-5-(3,4-dichlorophenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(4-methoxyphenyl)-1-(4-methylsulfonylphenyl)imidazole;

A3  
cont

4-chloro-5-(3-fluoro-4-methoxyphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(3-fluorophenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(3-fluoro-4-methylphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(2-fluorophenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-1-(4-methylsulfonylphenyl)-5-(4-trifluoromethoxyphenyl)imidazole;  
4-chloro-5-(6-methyl-3-pyridyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(2-fluoro-4-methoxyphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(3-chloro-4-methylphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(3-methoxy-4-methylphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(4-chlorophenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(6-chloro-3-pyridyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(2,6-dichloro-3-pyridyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(2-chloro-6-methoxy-3-pyridyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(5,6-dichloro-3-pyridyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-1-(4-methylsulfonylphenyl)-5-(4-propoxyphenyl)imidazole;  
4-chloro-5-(3,5-diethoxyphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(4-ethoxyphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-1-(4-methylsulfonylphenyl)-5-(4-nitrophenyl)imidazole;

13  
cont

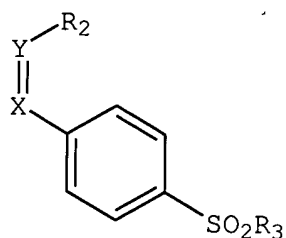
4-chloro-5-(4-methylsulfonylphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(4-ethylsulfonylphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(6-ethoxy-3-pyridyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-bromo-5-(4-fluorophenyl)-1-(4-methylsulfonylphenyl)imidazole;  
1-(4-fluorophenyl)-2-methyl-5-(4-methylsulfonylphenyl)imidazole;  
2-chloro-1-(4-fluorophenyl)-5-(4-methylsulfonylphenyl)imidazole;  
1-(4-fluorophenyl)-5-(4-methylsulfonylphenyl)imidazol-2-carboxaldehyde;  
methyl 1-(4-fluorophenyl)-5-(4-methylsulfonylphenyl)imidazol-2-carboxylate;  
2-bromo-1-(4-fluorophenyl)-5-(4-methylsulfonylphenyl)imidazole;  
1-(4-fluorophenyl)-5-(4-methylsulfonylphenyl)imidazol-2-carbonitrile;  
2-chloro-5-(4-methylsulfonylphenyl)-1-phenylimidazole;  
2-chloro-1-(4-methylphenyl)-5-(4-methylsulfonylphenyl)imidazole;  
4-[4-chloro-5-(4-fluorophenyl)imidazol-1-yl]benzenesulfonamide;  
4-(4-chloro-5-phenylimidazol-1-yl)benzenesulfonamide;  
4-[4-chloro-5-(3,4-dichlorophenyl)imidazol-1-yl]benzenesulfonamide;  
4-[4-chloro-5-(4-methylphenyl)imidazol-1-yl]benzenesulfonamide;  
4-[4-chloro-5-(4-ethoxyphenyl)imidazol-1-yl]benzenesulfonamide;  
4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]benzenesulfonamide;  
4-[4-chloro-5-(6-chloro-3-pyridyl)imidazol-1-yl]benzenesulfonamide;  
4-[5-(4-fluorophenyl)imidazol-1-yl]benzenesulfonamide;  
5-(4-aminophenyl)-4-chloro-1-(4-methylsulfonylphenyl)imidazole;  
5-(6-ethoxy-3-pyridyl)-1-(4-methylsulfonylphenyl)imidazole;

Q3  
amt

4-chloro-5-(4-dimethylaminophenyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(3-chloro-4-dimethylaminophenyl)-1-(4-methylsulfonylphenyl)imidazole;  
4-chloro-5-(3-chloro-4-dimethylaminophenyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(4-acetylaminophenyl)-4-chloro-1-(4-methylsulfonylphenyl)imidazole;  
5-(4-ethylsulfinylphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
5-(4-ethylsulfonylphenyl)-1-(4-methylsulfonylphenyl)imidazole;  
a salt thereof;  
a solvate thereof; and  
a prodrug thereof.

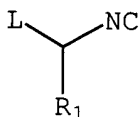
12. (Amended) A process for preparing a compound of formula I according to claim 1 which comprises:

(a) when in a compound of formula I  $R_1$  represents hydrogen or methyl, reacting an imine of formula II



II

wherein X, Y, R<sub>2</sub> and R<sub>3</sub> are as defined in claim 1, with an isocyanide of formula III

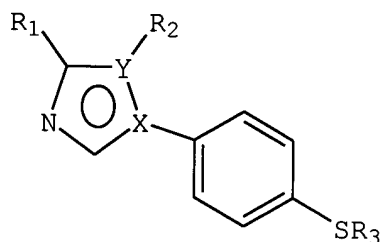


III

wherein R<sub>1</sub> represents hydrogen or methyl and L represents a leaving group; or

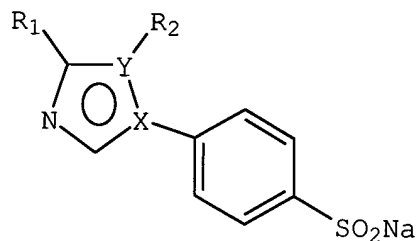
(b) when in a compound of formula I R<sub>3</sub> represents C<sub>1-8</sub> alkyl or C<sub>1-8</sub> haloalkyl, oxidizing a thioether of formula VIII,





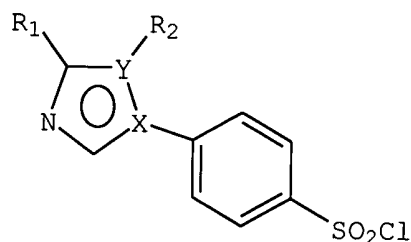
VIII

wherein  $R_3$  represents  $C_{1-8}$  alkyl or  $C_{1-8}$  haloalkyl and  $X$ ,  $Y$ ,  $R_1$  and  $R_2$  are as defined in claim 1, with an oxidizing agent; or  
(c) when in a compound of formula I  $R_3$  represents  $-NH_2$ , reacting a compound of formula IX



IX

wherein  $X$ ,  $Y$ ,  $R_1$  and  $R_2$  are as defined in claim 1, with hydroxylamine-*O*-sulfonic acid; or  
(d) when in a compound of formula I  $R_3$  represents  $-NR_4R_6$ , reacting a compound of formula XI



XI

wherein X, Y, R<sub>1</sub> and R<sub>2</sub> are as defined in claim 1, with an amine of formula HNR<sub>4</sub>R<sub>6</sub>; or

Q3  
concl (e) when in a compound of formula I R<sub>1</sub> represents halogen and X represents N, reacting a compound of formula I wherein R<sub>1</sub> represents hydrogen with a halogenating agent; or

(f) when in a compound of formula I R<sub>1</sub> represents halogen and Y represents N, reacting a compound of formula I wherein R<sub>1</sub> represents hydrogen with a strong base and a halogenating agent; or

(g) converting a compound of formula I into another compound of formula I.

---

**Added Claims:**

---

Q4 23. A process for preparing a salt of a compound of formula I according to claim 1 which comprises reacting a compound of formula I with an acid to give the corresponding acid addition salt.

24. A method of treating or preventing a disease mediated by cyclooxygenase in a mammal in need thereof, which comprises administering to said mammal a therapeutically effective amount

of a compound of formula I according to claim 1 or a pharmaceutically acceptable salt, solvate or prodrug thereof.

25. A method in accordance with claim 24, wherein said mammal is a human.

26. A method of treating or preventing a disease mediated by cyclooxygenase-2 in a mammal in need thereof, which comprises administering to said mammal a therapeutically effective amount of a compound of formula I according to claim 1 or a pharmaceutically acceptable salt, solvate or prodrug thereof.

27. A method in accordance with claim 26, wherein said mammal is a human.

all  
Gott  
28. A method of treating inflammation, pain or fever in a mammal in need thereof, which comprises administering to said mammal a therapeutically effective amount of a compound of formula I according to claim 1 or a pharmaceutically acceptable salt, solvate or prodrug thereof.

29. A method in accordance with claim 28, wherein said mammal is a human.

30. A method for inhibiting prostanoid-induced smooth muscle contraction in a mammal in need thereof, which comprises administering to said mammal a therapeutically effective amount of a compound of formula I according to claim 1 or a pharmaceutically acceptable salt, solvate or prodrug thereof.

31. A method in accordance with claim 30, wherein said mammal is a human.

32. A method of treating or preventing dysmenorrhea, preterm labor, asthma or bronchitis in a mammal in need thereof, which comprises administering to said mammal a therapeutically effective amount of a compound of formula I according to claim 1 or a pharmaceutically acceptable salt, solvate or prodrug thereof.

33. A method in accordance with claim 32, wherein said mammal is a human.

34. A method of treating or preventing cancer in a mammal in need thereof, which comprises administering to said mammal a therapeutically effective amount of a compound of formula I according to claim 1 or a pharmaceutically acceptable salt, solvate or prodrug thereof.

35. A method in accordance with claim 33, wherein said mammal is a human.

36. A method according to claim 34 or 35, wherein said cancer is a gastrointestinal cancer.

37. A method according to claim 36, wherein said cancer is colon cancer.

38. A method of treating or preventing cerebral infarction, epilepsy, or a neurodegenerative disease in a mammal in need thereof, which comprises administering to said mammal a